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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,210	03/09/2005	Evy Lundgren-Akerlund	10142.0004	4342

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,210	LUNDGREN-AKERLUND, EVY	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *5,7-14 and 16-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-18 are pending.

2. Applicant's election with traverse of Group 1, claims 1-4, 6 and 15 drawn to a method of identifying a mammalian mesenchymal stem cell using a marker comprising an integrin alpha 10 chain expressed on the cell surface of a mesenchymal stem cell or intracellular in mesenchymal stem cell as a marker for mammalian mesenchymal stem cells, wherein the expression is detected by an immunoassay filed on 12/4/06, is acknowledged.

Applicant's traversal is on the grounds that the instant application is a national stage filing under 35 U.S.C. § 371 and thus unity of invention practice applies to the application. To satisfy unity of invention, the claims must be united by a single inventive concept that contributes a special technical feature to the art. The claims of the instant application are all united by the single inventive concept of the use of integrin alpha 10 chain or integrin alpha 10 chain and integrin alpha 11 chain as a marker for mammalian mesenchymal stem cells. This inventive concept is a special technical feature that is unique to the art. Applicant concludes that the restriction is improper. Further, Applicant directs the Examiner's attention to MPEP 803, which sets forth the criteria and guidelines for Examiners to follow in making proper requirements for restriction (serious burden). This is not found persuasive because the composition of Group VIII does not have a common core structure or function because there is no 1:1 correlation between the composition and the claimed methods of Groups 1-7 and 9. Further, products (alpha 10 and alpha 11) are two proteins not one particular protein (see PCT Rule 13.2 and example 17 of Annex B) in MPEP. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 5, 7-14 and 16-18 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-4, 6 and 15 are under examination as they read on a method of identifying a mammalian mesenchymal stem cell using a marker comprising an integrin alpha 10 chain expressed on the cell surface of a mesenchymal stem cell or intracellular in mesenchymal stem cell as a marker for mammalian mesenchymal stem cells, wherein the expression is detected by an immunoassay.

5. Applicant's IDS, filed 12/08/04, is acknowledged.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4, 6 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1 and 15 provide for the use/utilize of alpha10 chain, but, since the claim does not set forth any steps involved in the method, it is unclear what method applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

B. It is unclear how the recited "detecting integrin chain alpha 10" in claim 3(b) and the recitation "detecting integrin chain alpha 10 protein expression" in claim 4 would happen in the absent of a contacting step. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 6 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for a method of using a marker comprising an integrin alpha 10 chain expressed on the cell surface of a mesenchymal stem cell or intracellular in a mesenchymal stem cell as a marker for mammalian mesenchymal stem cells in claim 1, wherein the integrin alpha 10 chain is expressed as a heterodimer in combination with an integrin beta 1 chain in claim 2, or a method for identifying a mammalian a mammalian mesenchymal stem cell in claim 3, or a method for identification of a mammalian mesenchymal stem cell, comprising ustilizing a marker comprising an integrin alpha chain expressed on the cell surface of a mesenchymal stem cell or intracellular in a mesenchymal stem cell in claim 15.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific

enablement is necessary in order to satisfy the statute. The claims encompass measuring integrin chain alpha10 in samples containing a mesenchymal stem cell as a molecular marker. However, the hMSC must express the marker recognized by the "antibody" in order for the method to work. The specification under example 3 (page 25) discloses detection of MSC expressing the integrin alpha10 from human colony-forming cells derived from human bone marrow. The Example in the specification discloses that colony-forming cells from human bone marrow express the integrin alpha10 represent a population of mesenchymal stem cells. Further, the influence of FGF-2 on alpha10 expression on hMSC was investigated. Cells treated with EGF-2 formed colonies typical of MSCs expressed the integrin alpha10 (see figure 4b), while the control did not. However, the control is the claimed mesenchymal stem cells, and the FGF-2 treated mesenchymal cells give a cell population with a robust chondrogenic response (giving rise to or forming cartilage) as is evidenced by Murdoch et al, (European Cells and Materials, 6(2):17, 2003). It seems that Applicant has identify a subpopulation of hMSC that express α10 chain. It is clear from Applicant example that the starting material (i.e., mesenchymal stem cells) do not express alpha 10 integrin on the cell surface (see Fig. 4). Yet, Applicant is claiming a method of utilizing alpha10 integrin a marker for MSC. It is not clear that osteogenic, myogenic, marrow stroma, tendogenic/ligamentogenic cells of the hMSC express alpha10 chain integrin.

The specification under Example 1 (page 22) discloses detection of integrin alpha 10 (intracellular) and integrin alpha11 chain on human MSC using immunoprecipitation technique. The result shows that hMSC in culture express both integrins alpha10 and alpha 11 on their surface. However expression of alpha 10 on the surface of the hMSC does not mean that it is a marker for hMSC, or alpha 10 can be use to identify hMSC. Several proteins (e.g., integrins, collagens and proteoglycans) are expressed on the surface of hMSC, that cannot be use as a marker for hMSC. It is not clear why the detection of alpha10 integrin can be use to identify hMSC, while the other expressed proteins cannot. Specially, since integrin chain alpha 10 as molecular markers for hMSC have failed to fulfill the requirements of a diagnostic and prognostic assessment. Lehnert et al (Cytogenet Cell Genet. 87:238-244, 1999) teaches that the expression pattern of integrin α10 subunit were widely expressed in a panel of 24 tissue types where the highest expression was found in muscle and heart (see abstract and Fig.5). Further, WO 99/51639 (IDS ref) publication teaches that analysis of the hybridized mRNA showed that α10 was expressed in aorta (normal nonatherosclerotic artery) (see pg. 25, lines 18-19 and Figure 12). While, US 2005/0255182 publication shows the detection of integrin alpha10 chain in an atherosclerotic plaque of a murine aorta. In particular, Fig. 2 shows the staining of the integrin alpha10 chain as a strong staining of the cell surface of a cell in the aortic plaque. Finally, Gullberg and Lundgren-Akerlund and Fig. 12 of the WO `639 publication show that the expression of α10 is not restricted hMSC but expressed on a few human tissues such as aorta, trachea, lung fetal lung kidney fetal kidney, heart fetal heart spinal cord, mammary gland, bone marrow small intestine and skeletal muscle (see Table 2, page 32).

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the

nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 1-4, 6 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/51639.

The WO `639 publication claims the using an integrin subunit α10 or binding entities having the capability of binding specifically to an integrin subunit α10 as a marker or target molecule of cells expressing integrin subunit α10 (see published claims 28, 43, 51), wherein said cells is osteoblasts (MSC) (published claims 34, 52 and 60 in particular). Further, the `639 publication teaches that the integrin subunit α10 is highly expressed in perichondrium and periostem (undifferentiated mesenchymal cells from the perichondrium) using α10-antibody that recognizing the cytoplasmic domain of α10 (see page 23, line 26 to page 24, line 5 and Fig. 9 in particular). The `639 publication further teaches the use of α10-antibody that recognizing the cytoplasmic domain of α10 stained osteoblast (mesenchymal stem cells) in the bone bark (see page 23, lines 26-37 in particular). The referenced method detect the integrin alpha 10 protein espression by an immunoassay (i.e., immunohistochemistry, see example 8 in particular). In addition, the `639 publication teaches that α10 integrin subunit is unreglated in the limb when the mesenchymal cells undergo condensation to form cartilage. Especially the edge of the newly formed cartilage has high expression of α10 (i.e., perichondrium and periosteum) (see page 24, lines 24, to 29 in particular). Also, the `639 publication teaches that expression of a10 was found in the fascia surrounding tendon and skeletal muscle and in the tendon structures in the heart valves (i.e., tendogenic cells) (see page 26, lines 4-6, in particular).

The `639 publication teaches that α10 was immunoprecipitated with β1 integrin. The `639 publication concludes that the α10 is a member of the β1-integrin family (i.e., form heterodimer) (see page 23, lines 1-5).

The scoring step in claim 3(c) would be inherent step in the referenced method.

The reference teachings anticipate the claimed invention.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 21, 2007

Maher Haddad

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